## REMARKS

Claims 1-22 are pending in the present application. No claim amendments are made and accordingly no new matter is inserted into the application.

***Request for Initialed Form PTO-1449***

In reviewing the application file, the undersigned has noted that the appropriate initialed Form PTO-1449 in response to the Information Disclosure Statement (IDS) filed on February 20, 2002 has not been received by Applicant. The Examiner is therefore respectfully requested to initial and return a copy of the Form PTO-1449 to the undersigned as soon as possible. A copy of the Form PTO-1449 originally filed on February 20, 2002 is attached hereto for the Examiner's convenience.

***Rejection under 35 U.S.C. § 103***

Claims 7-21 are rejected under 35 U.S.C. 103(a) for allegedly being obvious over Lucito et al. (*PNAS USA*, 95:4487-4492, 1998) in view of Thorstenson et al. (*Genome Research*, 8(8):848-855, 1998). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Lucito et al. discloses genomic "representations" made by PCR from nanogram amounts of restriction endonuclease-cleaved DNA that

has been ligated to oligonucleotide adaptors, wherein the genomic representations capture approximately 70% of the genome. Lucito et al. fails to disclose the shearing process. The Examiner attempts to correct this deficiency by combining therewith Thorstenson et al. Thorstenson et al. discloses a Hydrodynamic Process showing a high reproducibility of shearing. The Examiner asserts that it would be obvious to combine Thorstenson et al. with Lucito et al. to produce the present invention. Applicants respectfully disagree.

First of all, Applicants respectfully submit that even a hypothetical combination of Lucito et al. and Thorstenson et al. still fails to render the present invention obvious. Specifically, neither Lucito et al. nor Thorstenson et al. teach or suggest that the use of fragmented DNAs allows for the construction of a genomic DNA library that maintains copy numbers for a set of genes or sequences on the genome, wherein the fragmented DNAs have a distribution ratio of 1 to 5 as defined by the size ratio of the maximum size of fragmented DNA to the minimum size of fragmented DNA, and have a size convergence rate of not less than 80%. Further, Lucito et al. fails to disclose the means by which the above distribution ratio and size convergence rate are achieved. Even if these references were combinable, one of ordinary skill in

the art would generally arrive at a reproducible genomic "representation"

In any event, Applicants respectfully submit that the skilled artisan would never be motivated in the first place to combine Lucito et al. with Thorstenson et al. Thorstenson et al. discloses in line 19 of the right column of page 851 to line 15 of the left column on page 852 that Hydrodynamic Process-sheared DNAs having an average size of 3-6 kb resulted in a sequencing library wherein the cloned inserts have an average size of about 2.7 kb. Thorstenson et al. states that this small average size is probably attributable to bias for cloning smaller fragments. From the above facts, one of ordinary skill in the art would not expect that the use of Hydrodynamic Process-sheared DNAs would allow for the construction of a genomic DNA library that maintains the copy numbers for a set or genes or sequences on the genomic DNA, while also maintaining the abundance ratio of the set of genes or sequences on the genome.

Finally, the present invention exhibits excellent effects not seen in the cited prior art references. Tanabe et al., *Genes, Chromosomes & Cancer*, 38:168-176 (2003), attached hereto as Exhibit 1, illustrates the differences between the present invention and that of Lucito et al. and Thorstenson et al. and the significantly excellent effects of a library produced by the present invention versus a library prepared by endonuclease-based techniques. As

described in the left column, lines 9-12 of page 175, only 12 to 24 % of the genome was captured in a library by using known methods, including the method of Lucito et al. As noted in the specification, the method of the present invention allows for the maintenance of copy numbers for a set of genes or sequences on the genome, preferably 85% to 95% or more (see page 10, lines 10-15 of the specification). Thus, the present invention allows for an increased amount of genomic sequences not available with the methods disclosed in the prior art.

For all of the above reasons, Applicants respectfully submit that the present invention is not obvious over Lucito et al. and Thorstenson et al. Withdrawal of the instant rejection is therefore respectfully requested.

***Conclusion***

Applicants respectfully submit that the above remarks and/or amendments fully address and overcome the outstanding rejections and objections. For the foregoing reasons, Applicants respectfully request the Examiner to withdraw all of the outstanding rejections and objections, and to issue a Notice of Allowance indicating the patentability of the present claims. Early and favorable action of the merits of the present application is thereby respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of three (3) months to April 8, 2004, in which to file a reply to the Office Action. The required fee of $950.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,
BIRCH, STEWART, KOLASCH & BIRCH, LLP

By #28977
Marc S. Weiner, #32,181

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

MSW/KLR:gmh

Attachment(s): FORM PTO-1449
Exhibit 1: Tanabe et al., *Genes, Chromosomes & Cancer*, 38:168-176 (2003)